Analysis of Venous Thromboembolism Risk in Patients Undergoing Craniotomy

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■ OBJECTIVES: **Craniotomy poses a risk for postoperative venous thromboembolism (VTE), but the utility of anticoagulation in this patient population is unclear. We sought to identify risk factors predictive of VTE in patients undergoing craniotomy.**

■ METHODS: **The American College of Surgeons National Surgical Quality Improvement Project (ACS-NSQIP) database was reviewed for patients undergoing craniotomy. Clinical factors provided by the database were analyzed for association with VTE.**

■ RESULTS: **A total of 10,477 adult patients who underwent craniotomy from 2011–2012 were identified. The rate of VTE was 3.2% (pulmonary embolism [PE] was 1.3%; deep vein thrombosis [DVT] was 2.4%). Several factors were significant in univariate analysis, and a subset persisted after multivariate analysis. Patients were assigned a risk score on the basis of the presence of those variables. Higher risk scores were predictive of VTE risk, as well as increasing time from surgery to discharge and mortality. A receiver operating characteristics curve revealed a significant area under the curve (0.719) for scores being predictive of VTE risk. The model was validated against our similar analysis of 2006–2010 NSQIP data and demonstrated comparable findings.**

■ CONCLUSIONS: **The risk of postoperative VTE after craniotomy can be quantified by a simple risk score, with increasing risk factors conferring increased risk of VTE. On the basis of risk scoring, a subset of patients who would benefit from anticoagulation post craniotomy may be identified.**

INTRODUCTION

Modern medicine has largely succeeded in treating and extending the course of a number of chronic and degenerative conditions. The current era of medicine has shifted focus more from tertiary prevention to primary prevention and risk reduction. Pursuant with this focus, stakeholders seek to reduce expenses by limiting preventable causes of hospitalization and prolonged admissions. One arena for high-yield prevention and cost reduction is the perioperative period. The Surgical Care Improvement Project (SCIP) was started in 2006 with assistance from the Joint Commission with the goal of diminishing preventable complications before, after, and within the operative window. The instillment of recommendations regarding appropriate antibiotic and medication use, postoperative blood glucose measures, surgical site hair removal, urinary catheterization, temperature control, and prevention of venous

Key words
- Craniotomy
- Venous thromboembolism

Abbreviations and Acronyms
ACS-NSQIP: American College of Surgeons National Surgical Quality Improvement Project
AHRQ: Agency for Healthcare Research and Quality
ASA: American Society for Anesthesiologists
AUC: Area under the curve
CMS: Center for Medicare and Medicaid Services
CPR: Cardiopulmonary resuscitation
CPT: Current Procedural Terminology
CVA: Cerebrovascular accident
DVT: Deep vein thrombosis
HAC: Hospital-acquired condition
ICH: Intracranial hemorrhage
No.: Number
NQF: National Quality Forum
NSQIP: National Surgical Quality Improvement Project
OR: Odds ratio
PE: Pulmonary embolism
PNA: Pneumonia
RCT: Randomized controlled trials
ROC: Receiver-operating characteristics
SCIP: Surgical Care Improvement Project
TM&M: Thoracic Morbidity and Mortality System
UTI: Urinary tract infection
V-Q: Ventilation-perfusion
VTE: Venous thromboembolism

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thromboembolism (VTE) has materialized as a result. The Joint Commission, National Quality Forum (NQF), and Agency for Healthcare Research and Quality (AHRQ) support these quality measures and have created mandates for hospitals to report violations or else suffer financial penalties. In an effort to improve outcomes and avoid fines, hospitals have developed protocols to track these aforementioned measures. Yet there is no standard approach to determining risk of VTE and the benefit of prophylactic anticoagulation in at-risk populations (4).

Concerning VTE then, it comes as no surprise that surgeons especially are forced by institutional and financial pressures to tread delicately the line between thrombosis and hemorrhage. This dilemma is most pronounced in neurosurgical procedures. A meta-analysis of 8 randomized controlled trials (RCTs) found that for every 1000 craniotomy patients anticoagulated with heparin, 91 VTEs would be prevented, whereas 7 intracranial hemorrhages (ICH) and 28 minor bleeds would occur (15). Thus the suggested VTE rate is 9.1%, which appears high at face value but is explained in the meta-analysis. Three of 6 studies analyzed were completed before the use of routine mechanical prophylaxis and failed to include such treatment in control groups. Additionally, different methods of detecting VTE were used (including venography and I^{125} fibrinogen) that have higher sensitivity and likelihood of capturing asymptomatic VTEs. Therefore although the results seem to support anticoagulation, the authors concede that the absolute values may provide false assurance and VTE detection using surrogate markers may detect less worrisome, asymptomatic VTEs. When accounting for these low-risk VTEs the risk reduction of VTE and risk elevation of ICH may be comparable (15). However, those neurosurgical patients with confirmed VTE are more likely to suffer demise from pulmonary embolism (PE) rather than hemorrhage due to anticoagulation, so the decision to anticoagulate in this population is slightly clearer (9).

Rates of VTE and the benefit of aggressive prophylaxis protocols have been explored and proven beneficial in numerous subsets of neurosurgery patients, including post spinal surgery and in patients undergoing craniotomy for tumor (8, 9, 12). In the craniotomy for tumor subpopulation, risk factors of VTE have been identified using both national and institutional data (24, 35). Thus identification of risk factors of VTE among all craniotomies would allow anticoagulation to be targeted toward the most at-risk patient populations. The American College of Surgeons National Surgical Quality Improvement Project (NSQIP) (http://site.acsnsqip.org/) database provides a large number of craniotomy cases, which may elucidate populations at risk for VTE (18). Data recorded include comorbid conditions, preoperative, operative, and postoperative complications. We previously analyzed 2006–2010 NSQIP craniotomy data to elucidate factors associated with VTE and identify patients most likely to benefit from prophylactic anticoagulation. In fact, 2011–2012 NSQIP data are the most recent NSQIP data sets currently available and were not available at the time of our previous analysis. By analyzing 2011–2012 NSQIP data, we hope to validate our previous model and refine the risk score but also extend the model with additional analyses (23). A total of 4844 patients were included in NSQIP data from 2006–2010, whereas over 2011–2012 there were 10477 records. Thus identifying factors preserved across multiple years bolsters the analysis and increases the strength of our model.

METHODS

Baseline Univariate Analysis

A total of 10,477 patients from 2011–2012 underwent craniotomy on the basis of primary Current Procedural Terminology (CPT) procedure code. Ordinal and nominal variables were subjected to univariate two-tailed χ^2 analysis and Fisher's exact test when expected frequencies were low to identify clinical factors associated with VTE. All of the factors in the ACS-NSQIP data set were subjected to analysis. For univariate χ^2 analysis, original α was set at 0.05 and P values were adjusted using Holm-Bonferonni correction. Those factors less than their respective adjusted α were considered statistically significant, and odds ratios (ORs) were calculated when appropriate. Procedures performed for a tumor diagnosis were also identified on the basis of primary CPT code (61510, 61512, 61518, 61519, 61520, 61521, 61526, 61545, 61546, 61575). Many factors were converted to binary variables to assist in calculation of ORs.

Preoperative and intraoperative factors with P values <0.05 were subjected to a forward, stepwise, multivariate binary logistical regression analysis (entry level = 0.05, exit = 0.1) for the identification of factors independently correlated with VTE. Covariate interactions were analyzed with chi-square analysis, noted, and included stepwise in iterations of multivariate regression but failed to impact the robustness of the model. Similarly, postoperative factors were subjected to multivariate logistic regression with care taken to exclude patients in which the event of interest occurred after VTE. Again, covariate interactions were analyzed and included in multivariate regression but failed to impact the robustness of the model. Thirteen factors were included in the final multivariate model and were converted to a binary score of 0 or 1 with 1 representing presence of the factor. Goodness of fit of the multivariate logistic regression model was assessed using Hosmer-Lemeshow test where $P > 0.05$ indicates a model that fits the data well. The VTE risk score was compared with VTE rate, 30-day mortality, and days from surgery to discharge using a number of statistical tests including both linear and Cox regression.

A receiver operating characteristics (ROC) curve was used to assess predictive strength of VTE risk scores on the basis of reported area under the curve (AUC). AUC values greater than 0.70 represent acceptable discrimination, and values greater than 0.80 indicate excellent discrimination (7, 16, 32). For validation of the present analysis against past data, the cohort of 4844 patients undergoing craniotomy from 2006–2010 NSQIP data was used. The Cox proportional hazards regression model was an additional analysis conducted to examine the association of clinical factors with VTE in regard to time from surgery to discharge. All statistical analyses were performed using SPSS software version 18.0 (IBM, Armonk, New York, USA).

RESULTS

The rate of VTE in the cohort of 10,477 patients was 3.2% (PE was 1.3%; DVT was 2.4%). There were 131 patients in the cohort with a PE, of which 77 patients did not have an associated DVT (58.8%). VTE, DVT, and PE were all significantly associated with increased days from operation to discharge ($P < 0.001$). Additionally, VTE, DVT, and PE were all significantly associated with increased